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Do you think that tropomyosin and G_actinisoforms & tropomyosin isoforms with PPARs have strong relationships with the root of some diseasesas some kind of cancer diseases??

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I. Introduction

The binding of the myosin heads to the muscle actin is a highly regulated process. The thin filament is made of actin, tropomyosin, and troponin. The contraction of skeletal muscle is triggered by nerve impulses that in turn stimulate the release of Ca2+. The release of Ca2+ from the sarcoplasmic reticulum causes an increase in the concentration of Ca2+ in the cytosol. Calcium ions then bind to troponin, which is associated with tropomyosin. Binding causes changes in the shape of troponin and subsequently causes the tropomyosin isoform to shift its position on the actin filament.

And, globules consists of two lobes separated by a cleft. This structure represents the "ATPase fold", which is a centre of enzymatic catalysis that binds ATP and Mg2+ and hydrolyzes the former to ADP plus phosphate.

That when phosphate gps deficiency appeared and +ve molecules increased in tissues will reflect the dysfunction of G-actin and tropomyosin that lead to tumor in that tissue spot !! And also, will be the main reason for Atherosclerosis and their obstructions!!

Tropomyosin 3, an isoform that is not normally expressed in neuronal cells, was broadly distributed throughout the neuron, while exogenous expression of the neuronal isoform Tropomyosin 5NM1/2 was found to sort to the growth cone of neurons as does the endogenous Tropomyosin 5NM1/2. As these two transgenes differ only in the tropomyosin coding region yet are localized in two distinct areas, the findings suggest that, in addition to mRNA sorting, the proteins themselves contain sorting information.

Abstract :

There are a strong relationship between the process of tropomyosin isoform sorting and the incorporation of tropomyosin isoforms into organized arrays of actin filaments. There is no evidence for active transport of tropomyosin isoforms to specific locations.

As ATP functions decreased which located in G_ actin, as cells cleaning and metabolism will decreased as the tropomyosin genes functions will decrease and the tropomyosin isoforms functions will decrease too lead to accumulation of proteins in that ares& lead to decreasing in the transfer of sensations to the nervous system, and neuron leads to the decreasing in the transmission of messages to the brain.

Tropomyosin 3, an isoform that is not normally expressed in neuronal cells, was broadly distributed throughout the neuron, while exogenous expression of the neuronal isoform Tropomyosin 5NM1/2 was found to sort to the growth cone of neurons as does the endogenous Tropomyosin 5NM1/2. As these two transgenes differ only in the tropomyosin coding region yet are localized in two distinct areas, the findings suggest that, in addition to mRNA sorting, the proteins themselves contain sorting information.

there are only six actin isoforms, and these isoforms are responsible for an array of unique and complex cellular structures and key cellular interactions. It is thought that the function and form of the actin cytoskeleton is controlled largely by actin-binding proteins (ABP) that are associated with the actin polymer. ABP are a group of proteins that bind to actin. Although tropomyosin is sometimes included as an ABP, it is not a true ABP.

G-actin has a globular structure; however, X-ray crystallography shows that each of these globules consists of two lobes separated by a cleft. This structure represents the "ATPase fold", which is a centre of enzymatic catalysis that binds ATP and Mg2+ and hydrolyzes the former to ADP plus phosphate, plus is responsible about G_protein functions. The presentation of the "ATPase fold" in G_actin structure indicates the responsibility of ATPase for G_actin and for tropomyosin .

In skeletal muscles, any deficiency in G_actin functions which include ATPase isdue to increasing in +ve molecules morethan their normal % that will lead to decreasing in muscles functions including arteries contacts and functions. That dynamic interactions(due to polaritésproductions system) between the thick and thin filaments alpha subunits is the results in muscle contraction and biological activities in that tissue for itself & for communication with other tissues .

Myosinis strongly related to and controlled by Ca +veelements and by the concentrations of ATPase enzymewhich present in G_actinalpha subunitsfilaments , and belongs to a family of motor proteins, and the muscle isoforms of that family comprise the thick filament. The thin filaments is made of skeletal muscle isoforms of CYP3A will actins.

Each myosin protein 'paddles' along the thin actin filaments , repeatedly binding to myosin-binding sites along the actin filaments thatby helping the polarités characters will let to go but in the presence of extra of +ve elements will be stabilized till will lead to hardness in tissue .

Also myosin is related to the concentration of the presence of +ve molecules that if increased will affect on ATPase &GTPase activities thattheir activities will be reduced or will be completely inhibited that will lead to decreasingin Muscles& arthritis suppleness thatmay will not contract , and willlead to roughness in the joints.

ipoproteins are divided into 5 major classes: chylomicrons, very low density lipoproteins (VLDL), intermediate density lipoproteins (IDL), low density lipoproteins (LDL) and high density lipoproteins (HDL). LDL and HDL are known as the “bad” and “good” cholesterol, respectively.

The levels of lipoproteins are strongly linked & related to the concentration level of ATPase &GTPase and their substrates in tissues & their cells, & elevated levels of LDL are linked to premature development of atherosclerosis and coronary heart disease.

The deficiency in ATPase enzyme and its substrates in myosin and tropomyosin will lead to decreasing in tropomyosin isoforms production and may disorder in their genes structures and The cells will not perform their functions successfully and will not clean up their toxins products resulting from their Metabolism, that will leads to deposits those products while they are running (red blood cells) through the arteries.

NGF is one of many inflammatory mediators that facilitate pain sensitization. It is released from mast cells along with other pro-inflammatory cytokines such as histamine and interleukins. At the peripheral nociceptor, NGF binds to tropomyosin receptor kinase A (TrkA) to facilitate pain sensitization in the periphery, and send that pain sensation in genes formsbonded with ATP and GTP forfast transport to brain then to neurons for receiving the answers from them for recoveries and protections if possible .

genes which responsible for generating more than 40 different tropomyosin isoforms, are related to NGF is one of many inflammatory mediators that facilitate pain sensitization, that any changes in tropomyosin genes sequences will change their isoforms structure then the binding with NGF will inhibit or not fully decreased result of un transport pain sensation and result of dysfunction in this part of tissue connected to their mast cells that result of dysfunction in T-cells synthesis due to originally changing in tropomyosin isoforms synthesis that will lead to isolation to that part of tissue cells.

Categorization of tropomyosin's coiled-coil describes a unique pattern of amino acids within the primary structure of the alpha helices that comprise the dimer interface. The unique amino acid pattern, found within all coiled-coil proteins, is a heptad repeat, which follows a similar pattern to: H-P-P-H-C-P-C, where H is hydrophobic, P is polar and C is charged. That tropomyosin genes are producing their isomers that from their functions is to feed tropomyosin alfaamino acids to perform their functions for sensations andneuron conduction andalso those isoforms are so necessary for alpha tropomyosin amino acids recoveries at the time of inflammation and pains too.

The amino acids from each alpha chain interact with each other uniquely in that side chains for conferming with each other that they are in right séquences in their chains, but any changes will be recovered by their tropomyosin isoforms which will work as mRNAs,but, pain sensation will be migrated& transfer to neurons & brainby electron transfer which are active due to presenceof polarities, but when polarities increases than normal will increasethe ATPase activities thatwill increase translations and transcriptions in the favor of tissue that will release extra energy and more polarities that will be by ATP cycles and for supporting other tissues eg heart . Polarities decreased in the increasing of +ve elements as Ca+.

Tropomyosin genes , as mentioned , with help of their isoforms will form a long polymer along the length of actin in a head-to-tail overlap. This overlap region occurs as the amino acids from the N-terminus of one dimer overlaps with the amino acids of the C-terminus of another dimer by the help of polarities occurrence and theirelectronic active interactions . There are several intermolecular contacts in the overlap region, which consist of ionic, hydrophobic and non-polar interactions.

Thenon polar interactionbetween amino acids in alpha helices are occurred due to presence or increasing in+ve molecules or elements that are limited by presence of specific % of +ve elements to preventor

reduce hydrophobic orhydrophilicforstabilities of that régionor that part of alpha active chain (Note: many of the methionine residues interacting between the dimers are selenomethionineand those methionine amino acids are the main nucleotides in both Pentapeptides in enkephalin in brain.

Tropomyosin &Actin is not only essential component of the Cytoskeletonbut also so essential compositionof neuron & brain for their full functions, protections and recoveries, and playcrucial roles in thefeeding back by neuron for the right sequences for translations and transcriptions for all neurons activities in favor of normal living cells in all eukaryotic including heart and brain . The actin cytoskeleton functions in the generationareprotections, and maintenance of cells morphology and polarities too , in endocytosis and intracellular trafficking, in contractility, motility and cell division.

In cells, the assembly and disassembly of actin filaments, and also their organisation into functional higher-order networks, is regulated by tropomyosin main genes & their isoforms and (thatincludes the actin-binding proteins & ATPase).

I would like to answer this question :what are the main elementsor molecules that imp for increasing living cells polarities?, ATPase enzyme (which involves in tropomyosin & G-actin) and its substrates &GTPaseare the main in neuron in human body for causing and increasing polarities in cells tissues and also presence of Fluorine are so helpful for doing the same functions which is imp for insulin hormones synthesis in human. But polarities are signs of themetabolic cycles activities in cells andtissues and tissues &refer to thereactions of enough oxygen& phosphorus, related to presenceof enough fluorine specific %of +vemolor elements as Ca+ which the importance of presence of+veelements is just for stability of alpha subunits against polarités and hydrophobic, (that stabilities in alpha subunits for helping continually translations & transcriptions for brain functions and protecting heart functions in heart cells).

Also, polarités are imp for communications betweencells & tissues by delivering pain sensation, including sending & receiving massages to & from brain & neuron cells.

II. Result

The tropomyosin isoforms are influenced by the active actin isoformscompositions of microfilaments that their compositions and arrangements of their amino acids are complementary to some each others& for helping sending and receiving messages to & from brain & to neuron cells and heart. We can consider that complementary composition as a strong micro_ system for organizing, translations , and protecting tissue cells , and are the basis for linking cells together inthe same tissue and with other tissues for organizing the interactions betweenadjacent cells and in nabour areas in favorof poorsick cells. Means, if we inject imp molecules in one tissue those molecules will be moved to the poor cells(throughhelping from active polaritiesby translations and transcriptions depending on the avaliablities of amino acids units during movement) through cells & tissuesby actin filamentsand tropomyosin isoforms activities till will arrive to sick cells . Any changes in tropomyosin isoforms & G-actin compositionswill affect on cells conductivity and will affect on the deliveries molecules between cells and tissues and will affect on delivering sensation to brain, heart, and neuron cells .

Thatthe decreasing in G-actinand tropomyosinpolaritieswill lead to accumulation of biological molecules andprotein +ve molecules in tissues . Also, increasing of +ve biological molecules (whatever protein or others) more than normal logic %in the alphafilamentssubunits will inhibit allkind of sensation,andwill inhibit Communications and the links between cells and will cause Sedimentation of particles in that region .

NGF binds to tropomyosin receptor kinase A (TrkA) to facilitate pain sensitization, and to be always in polaritiesactive status for delivering sensations and receive molecules from others for their main local metabolic cycles and for surrounding cells communications and for their functions including local cells functions. When Tropomyosin receptor kinase A (TrkA) inhibited by increasing in +ve elements or changed in their amino acids chains sequences (identities and qualities) sensations will not deliver, isolations of those cells will occur and tumor appearance will start then will grow in this area as the original translated molécules will not arrive to those cells ten full cancer will start.

It has been reported that :''High-grade astrocytomas and glioblastomas are usually unresectable because they extensively invade surrounding brain tissue. That Signal regulatory protein (SIRP) α1 is an immunoglobulin superfamily transmembrane glycoprotein that is normally expressed in subsets of myeloid and neuronal cells. Transfection of many cell types with SIRPα1, including glioblastomas, has been shown to inhibit their proliferation in response to a range of growth factors''.

But, my answer is :

the High-grade astrocytomas and glioblastomas are due to increasing in +ve molecules in tissue specifically in actin filament alpha subunits that are blocking ATPase functions which involved in G-actin, lead to accumulation of biological molecules in that tissue without followingmetabolic cycles lead to a blocking deliveries the sensations including pain deliveries, and after time will lead tofullseparation of that tissue and its G_actin filaments will be Paralysised, and it can happen in arteries, in heart, in brain, and in someparts of inmyeloid(that can cause blood cancers too),and in neuronal cells too. That Signal regulatory protein (SIRP) α1

willbe inhibited due to inhibition in ATPase functions which involved in G_actin filaments that'll lead to accumulations of bio molecules with the molecules which early expressed for that tissue without migrations"*egpresence of (SIRP)alpha 1 in brain cancer and in some neuron cells tumortissue that have been migrated from myeloid for brain & neuron then blocked and accumulated with other mol cover and hardening that region*". The encoded protein byCD44 which is a receptor for the C-terminal cell binding domain of thrombospondincan be found in tumor cells due to the same reason of the inhibition&paralysis of G_actinsfilaments and theiroverlapped tropomyosin isoforms due to the inhibition of ATPase and increasing in Ca+in their alpha subunits .

mTOR Serine/threonine ormethionine protein kinase which is a central regulators of cellular metabolism, growth and survival in response to hormones, growth factors, nutrients, energy and stress signals.

mTORMéthioninekinase candirectly or indirectly regulates the phosphorylationsprocessesin and surrounding G_actin filaments and will perform the ATPase which inhibited in G actin filaments and in tropomyosin isoforms .

I think & believe that Peroxisome proliferator-activated receptor (PPAR) has strong rules for tropomyosin genes synthesis and G_actin isoforms synthesis, and activated kinase synthesis (including mTOR kinases) which needed for G-actin & tropomyosin functions. .
That PPAR has three forms structures :
PPARα – chromosome 22q12-13.1 (OMIM 170998)
PPARβ/δ – chromosome 6p21.2-21.1 (OMIM 600409)
PPARγ – chromosome 3p25 (OMIM 601487).

That the disorders of all PPARs have been described, generally leading to a loss in function and concomitant lipodystrophy(means dysfunction in ATPase which involved in G-actin filaments, and seems to me that disorder of PPAR leads to inhibition in G-actin genes & isoforms) , insulin resistance (also means there are disorders in translations processes across antigen & cell membrane will lead to disorder in tropomyosin genes and G_actin filaments isoforms and may disappearance in methionine &theirmethionine kinases imp structures that willinhibit polaritésand will isolate those cells & with not be able to react with insulin due to their isolation and disorder in their surroundings microfilamentous s genes .

Tropomyosin isoforms that is not normally expressed in neuronal cells, was broadly distributed throughout the neuron, why, & what it mean to all of us ?? Absolutely now I can say & report that tropomyosin & actin isoforms are playing the main roles for fertilization &specific way of protections & maintenance of the synthesis for all neuron cells and their functions . The dynamic remodeling of the tropomyosin isoforms &actin filaments cytoskeleton areso imp & play so essential roles for all essential roles in many cellular processes, including cell motility, delivering sensation to brain and all neuron cells, and play imp roles in protection &maintenance of living cells,and cytokines is. .
Imp to add that :
Increased ionic strength resulting from Na, potassium, Mg salts has shown to destabilize aa-tRNA acyl bond & the Increased pH also destabilize too,& increase the risk of cancer problems .
But Phosphate gps&Fluorine in biological genes SHOWE increasing in aa-tRNA stabilities, & consequently increasing in amino acids synthesis& ribosome activities, increase microfilaments G-actin functions, and decrease the risk of cancer .
Also, aminoacyl-tRNAsynthetase activates the binding of an amino acids with ATP thatincrease polarités in microfilaments G-actin that increase communications activities between cells and increasesensation delivers & conducting to neurons & catalyzes the transfer of activated aminoacyl-adenylate to 3′ end of its cognate tRNAs1,synthesizing an aminoacyl-tRNA that enters ribosome at a codon position that matches anticodon&prevent heart attack .

RNA cytosine methylation by Dnmt2 and NSun2 promotes tRNA stability & protein synthesis. But in theavaliablities of ATPase proper %functions. But, thepolarities that control the amount of bonding energy in cytosine-C5 promote aa-tRNA synthesis& functions, andtheirbinding with ATP by ATPase activities. also the values of Cytosine bonding energy define & limit the length of aa-tRNAs& its modificated function with ribosome and with antigen .

Also : activating acetylcholine synthesis from acetyl-coenzyme A, by activating acetyltransferase is depending on the polarities which mainly produced by microfilaments G-actin & tropomyosin isoforms, and dependingon functions of active aa-tRNAs cycles within cells and in plasma , that will
_increase immune efficienc
_Dissolve

Solid fatty acids _Dissolve solid proteins
_remove arterial occlusion
_preventing heart attack in the presence of right % of GTP & ATP .
Parathyroid hormone slightly increased expression of IL-6 mRNA in the avaliablities of phosphatase activitieswhich help to increases the polarities in biological molecules for helping G_actin and tropomyosin isoforms functions & conductivities and neuron cells and that help to increase the collagen synthesis in MC3T3-E1 cells.

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